For example, in certain aspects of the present invention, a sample is collected from a patient suspected of having an inflammatory disease or diagnosed with an inflammatory disease and PGE_2-EA in the sample is detected and measured. The amount of PGE_2-EA present in the sample correlates with COX-2 activity in the patient and is a marker of the progress or severity of that disease or disease process. In another example, a series of samples are collected from the patient over a period of time. During that period of time, the patient undergoes treatment for the inflammatory disease. Changes in the amount of PGE_2-EA measured over time are indicative of changes in COX-2 activity and changes in the patients disease state. This information would be used by the physician to evaluate the patient's condition as well as the effectiveness of therapeutic intervention, wherein a decrease in the PGH_2-EA metabolites or COX-2 activity is indicative of an improvement in the patient's condition or effective therapy.

PTO/SB/21 (09-04)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

4.6 COX-2 AND CANCER

Studies in human colon cancer have shown that COX-2 expression is increased in colon cancer cells compared to the adjacent colonic mucosa; similar observations have been made in experimental models of colon cancer (Eberhart, CE, *et al.* 1994, *Gastroenterology* 107:1183; Sheng, H, *et al.* 1997, *J. Clin. Invest* 99:2254; DuBois, RN, *et al.* 1996, *Gastroenterology* 110:1259). COX-2 expression is a marker for the metastatic potential of colon cancer cells and is related to patient survival (Tsujii, M, *et al.* 1997, *Proc. Natl. Acad. Sci. USA* 94:3336; Sheehan, KM, *et al.* 1999, *JAMA* 282:1254). In one study, for example, COX-2 expression was determined in 76 patients with a variety of stages of colorectal cancer (Sheehan, KM, *et al.*, 1999, *JAMA* 282:1254). Such studies can be used to generate a standard curve for COX-2 expression in cancer and colon cancer in particular (see *supra*).

Ten-year survival was significantly higher in patients with the lowest levels of COX-2 expression (68 versus 35 percent). These findings suggest that COX-2 activation promotes tumor growth. Consistent with this hypothesis is a study in which human colon cancer cells that expressed high levels of COX-2 were implanted into nude mice. Treatment with a selective COX-2 inhibitor reduced tumor formation by 85 to 90 percent and inhibited colony formation of cultured cells (Sheng, H, *et al.* 1997, *J. Clin. Invest* 99:2254). This benefit was not seen with tumor cells that lacked COX-2.

Certain aspects of the present invention include methods of detecting a tumor in a patient in need thereof, comprising: obtaining a sample from the patient and detecting at least one PGH_2-EA metabolite in the sample (for instance, see Example 5). The presence of the PGH_2-EA metabolite in the sample is a marker for the presence of the tumor in the patient. More preferably, an amount of PGH_2-EA metabolite detected in the sample of the patient will be measured, wherein the amount of PGH_2-EA metabolite measured is indicative of the amount or severity of tumor present in the patient.

A further aspect of the present invention is a method of measuring and monitoring the size, grade, and/or stage of a tumor, comprising: collecting a first sample of a subject and measuring the amount of PGH_2-EA metabolites in the first sample. Then a period of time is allowed to pass, during which the subject may, or may not, undergo anti-cancer therapy. After the period of time has passed, a second sample is collected from the subject and the amount of PGH_2-EA metabolites in the second sample is measured. The amounts of the PGH_2-EA metabolites in the first and second samples are compared, wherein the difference between the amounts of PGH_2-EA metabolites in the two samples is indicative of changes in the metabolism of the cancer cell.